PRINCIPLES OF INFECTIOUS DISEASE EPIDEMIOLOGY

MODULE II – THE INFECTIOUS DISEASE PROCESS

This outline is provided as an aid to the student. It contains only the basic content of the module. To view the supporting material such as graphics, examples, etc. please see the module itself.

I. INTRODUCTION

Module II is designed to prepare public health workers to meet the following objectives:

1. Describe the six major components of the infectious disease process
2. Demonstrate understanding of the concepts of the infectious disease spectrum

II. THE CHAIN OF INFECTION

In order for infection and disease to occur in an individual, a process involving six related components must occur. This process has been referred to as the "Chain of Infection." The six steps or "links" in the chain are:

- Etiologic agent
- Reservoir
- Portal of Exit
- Mode of Transmission
- Portal of Entry
- Susceptible Host

In this module, we will examine each of these links and some other important concepts that help us understand infectious disease transmission. To stop the spread of disease, one or more of these links must be broken.

A. Etiologic Agents

There are seven categories of biological agents that can cause infectious diseases. Each has its own particular characteristics. The types of agents are:

1. Metazoa
2. Protozoa
3. Fungi
4. Bacteria
5. Rickettsia
6. Viruses
7. Prions

1. **Metazoa** are multicellular animals, many of which are parasites. Among the diseases they cause are:

a. Trichinellosis, also called trichinosis, caused by an intestinal roundworm transmitted through undercooked meat.
b. Hookworm, transmitted through feces-contaminated water and soil. Infestation can cause chronic anemia that often results in retarded mental and physical development of children.
c. Schistosomiasis, caused by a blood fluke and transmitted through contaminated water. Symptoms are related to the number and location of eggs in the human body, and may involve the liver, intestines, spleen, urinary tract, and reproductive system.

2. **<u>Protozoa</u>** are single-cell organisms with a well-defined nucleus. Some of these are human parasites. Examples of diseases cause by protozoa include:
   a. Malaria, a mosquito-borne disease that is one of the top three infectious diseases in the world (along with tuberculosis and HIV).
   b. Giardiasis, an infection of the upper small intestine that causes a diarrheal illness. Outbreaks can be difficult to control, especially in child care settings
   c. Toxoplasmosis, transmitted to humans from cats and undercooked meat. When this systemic disease infects a pregnant woman, it can cause the death of the fetus.
   d. Pneumocystis carinii pneumonia or PCP, which is often fatal, especially in people with compromised immune systems such as those infected with HIV.

3. **<u>Fungi</u>** are nonmotile, filamentous organisms that cause diseases that can be very difficult to treat. Some examples important to public health are:
   a. Histoplasmosis, transmitted by inhaling dust from soil that contains bird droppings. The severity varies widely, with the lungs the most common site of infection.
   b. Candidiasis, transmitted by contact with human patients and carriers. This fungus causes lesions on the skin or mucous membranes, including “thrush” and vulvovaginitis. Symptoms can be severe in immunocompromised people.

4. **<u>Bacteria</u>** are single-celled organisms that lack a nucleus. They are responsible for a wide range of human diseases, including:
   a. Tuberculosis, a chronic lung disease that is a major cause of disability and death in many parts of the world.
   b. Staphylococcal disease, which can affect almost every organ system. Severity ranges from a single pustule of impetigo, through pneumonia, arthritis, endocarditis, etc., to sepsis and death.
   c. Chlamydia and gonorrhea, the most widespread sexually transmitted diseases.
   d. Tetanus and diphtheria, two diseases that were once major public health problems but are now well controlled through immunization.
   d. Other vaccine-preventable diseases caused by bacteria are:
      - Pertussis
      - Haemophilus influenzae type b (Hib)
      - Pneumococcal disease.

5. **Rickettsia** are a genus of bacteria usually found in the cells of lice, ticks, fleas and mites. They are smaller than most bacteria and share some characteristics of viruses. Diseases cause by rickettsia include:

a. Rocky Mountain Spotted Fever, a tick-borne systemic disease that can be hard to diagnose and that leads to death in 3-5% of US cases.

b. Typhus, a louse-borne rash illness with a high case-fatality rate that has occurred historically in poor living conditions brought on by war and famine.

6. **Viruses** are very small, consisting of an RNA or DNA core and an outer coat of protein. They can reproduce and grow only inside of living cells. Many viral illnesses are significant to public health, including:

a. Influenza, a respiratory illness that contributes to development of pneumonia and occurs in annual epidemics during the winter months

b. HIV (human immunodeficiency virus), that causes Acquired Immunodeficiency Syndrome (AIDS). This severe, life-threatening pandemic disease has spread worldwide within the past 20-30 years.

c. Rabies, that is spread to humans from animal bites or scratches. Rabies is almost always fatal in humans but is preventable by a vaccine.

d. Measles, mumps, rubella, and poliomyelitis are all well controlled in the US through immunization.

7. **Prions** are infectious agents that do not have any genes. They seem to consist of a protein with an aberrant structure, which somehow replicates in animal or human tissue. Prions cause severe damage to the brain. Diseases associated with prions include:

a. CWD, chronic wasting disease of mule, deer and elk;

b. BSE, bovine spongiform encephalopathy in cows; and

c. CJD, Creutzfeld-Jacob disease in humans.

[

B. Reservoirs

The next essential link in the chain of infection is the reservoir, the usual habitat in which the agent lives and multiplies. Depending upon the agent, the reservoir may be:

- humans,
- animals, and/or
- environment

When working with any disease agent, it is important to learn about its usual reservoir(s).

1. Human Reservoirs

There are two types of human reservoirs, acute clinical cases and carriers.

a. Acute clinical cases are people who are infected with the disease agent and become ill.

- Because they are ill, their contacts and activities may be limited.

- They are also more likely to be diagnosed and treated than carriers are.

b. Carriers, on the other hand, are people who harbor infectious agents but are not ill.
    - Carriers may present more risk for disease transmission than acute clinical cases, because their contacts are unaware of their infection, and their activities are not restricted by illness.
    - Depending on the disease, any of the following types of carriers may be important:
        - Incubatory carriers
        - Inapparent infections (also called subclinical cases)
        - Convalescent carriers
        - Chronic carriers

<u>Incubatory carriers</u> are people who are going to become ill, but begin transmitting their infection before their symptoms start. Examples: measles: a person infected with measles begins to shed the virus in nasal and throat secretions a day or two before any cold symptoms or rash are noticeable. Many other diseases also have an incubatory carrier phase. Most notably, HIV infection may be present for years before the person develops any symptoms.

<u>Inapparent infections</u>: People with inapparent infections never develop an illness, but are able to transmit their infection to others. With some diseases, inapparent infections are more common than acute clinical cases. Example: Of every 100 individuals infected with the poliomyelitis virus, only one becomes paralyzed. Four others will have a mild illness with fever, malaise, headache, nausea and vomiting. But 95 out of the 100 will have no symptoms at all, although they pass the virus in their feces.

Sometimes the likelihood of an inapparent infection depends on another epidemiologic factor, such as age. Hepatitis A is a good example of this. Over 50% of adults infected with this virus develop symptoms. However, among children under 5, there may be 10 inapparent infections for every child who develops jaundice. So children are very effective spreaders of the hepatitis A virus, which is passed in the feces regardless of the presence of symptoms.

<u>Subclinical infections</u>: With some diseases, such as meningococcal meningitis, the number of subclinical cases may be quite high before a single clinical case appears. On some military bases where outbreaks have occurred, the carrier rate has been documented at 50% or more.

Convalescent carriers are people who continue to be infectious during and even after their recovery from illness. This happens with many diseases. Example: Salmonella patients may excrete the bacteria in feces for several weeks, and rarely even for a year or more. This is most common in infants and young children. Treatment with inappropriate antibiotics may prolong the convalescent carrier phase.

Chronic carriers are people who continue to harbor infections for a year or longer after their recovery. Example: the chronic carrier state is not uncommon following hepatitis B infection, whether or not the person became ill, and may be lifelong. The risk of developing chronic hepatitis B depends on the person's age at infection. About 90% of infants infected at birth become chronic carriers of the disease, compared with only 1-10% infected after age 5. That is why it is so important to give hepatitis B vaccine to newborns.

2. **Animal Reservoirs**

Animal reservoirs of infectious agents can be described in the same way as human reservoirs. They may be

- acute clinical cases, or
- carriers.

Depending upon the disease, different carrier phases may be important in transmission.

3. **Environmental Reservoirs**

Plants, soil and water may serve as the reservoir of infection for a variety of diseases.

- Most fungal agents (mycoses) live and multiply in the soil.
  Examples:
  - The organism that causes histoplasmosis lives in soil with high organic content and undisturbed bird droppings.
  - The agents that cause tetanus, anthrax and botulism are widely distributed in soil.
  - The agent of Legionnaire's Disease lives in water, including hot water heaters.

C. Portal of Exit

The next link in the chain of disease transmission is the portal of exit, **the route by which the disease agent may escape from the human or animal reservoir**. While many disease agents have only one portal of exit, others may leave by various portals.

The portals most commonly associated with human and animal diseases are:

- Respiratory
- Genitourinary
- Alimentary
- Skin
  Superficial lesions

Percutaneous
- Transplacental

1. **Respiratory**: This is the route of many disease agents that cause respiratory illnesses such as the common cold, influenza, and tuberculosis. It is also the route used by many childhood vaccine-preventable diseases, including measles, mumps, rubella, pertussis, *Haemophilus influenzae* type b (Hib), and pneumococcal disease. This is the ***most important portal and the most difficult to control***.

2. **Genitourinary**: This portal of exit is the route of sexually transmitted diseases, including syphilis, gonorrhea, chlamydia, and HIV. Schistosomiasis, a parasitic disease, and leptospirosis, a bacterial infection, are both spread through urine released into the environment.

3. **Alimentary**: The alimentary portal of exit may be the mouth, as in rabies and other diseases transmitted by bites. More commonly, disease agents are spread by the other end of the intestinal tract. These are referred to as enteric diseases. In general, enteric diseases may be controlled through good hygiene, proper food preparation and sanitary sewage disposal. Examples include:
- Hepatitis A
- Salmonella, including typhoid
- Shigella
- Cholera
- Giardia
- Campylobacter

4. **Skin**: Skin may serve as a portal of exit through superficial lesions or through percutaneous penetration.
    - Superficial skin lesions that produce infectious discharges are found in smallpox, varicella (chickenpox), syphilis, chancroid, and impetigo.
    - Percutaneous exit occurs through mosquito bites (malaria, West Nile virus) or through the use of needles (hepatitis B and C, HIV).

5. **Transplacental**: This portal of exit from mother to fetus is important in the transmission of rubella, HIV, syphilis, and cytomegalovirus (the most common infectious cause of developmental disabilities). It is, fortunately, not a factor for most diseases.

D. Mode of Transmission

A mode of transmission is necessary to bridge the gap between the portal of exit from the reservoir and the portal of entry into the host. The two basic modes are **direct** and **indirect**.

1. **Direct transmission** occurs more or less immediately. Many diseases are transmitted by direct contact with the human, animal or environmental reservoir. Prime

examples are sexually transmitted diseases and enteric diseases such as shigella, giardia and campylobacter. Contact with soil may lead to mycotic (fungal) diseases.

Droplet spread is also considered direct transmission. Infectious aerosols produced by coughing or sneezing can transmit infection directly to susceptible people up to three feet away. Many respiratory diseases are spread this way.

2. **Indirect transmission** may occur through animate or inanimate mechanisms.

- *Animate mechanisms* involve vectors. Flies may transmit infectious agents such as shigella in a purely mechanical way, by walking on feces and then on food. Mosquitoes, ticks or fleas may serve as reservoirs for the growth and multiplication of agents, for example in malaria or Lyme disease.

- *Inanimate mechanisms*: When disease agents are spread by environmental vehicles or by air, this is referred to as indirect transmission by *inanimate mechanisms*. Anything may be a vehicle, including objects, food, water, milk, or biological products.
    - Food is a common vehicle for salmonella infections
    - Water is the usual vehicle in cholera outbreaks
    - Surgical instruments and implanted medical devices may be the vehicles of staphylococcal infections

  Indirect, airborne transmission is important in some respiratory diseases. This occurs when very tiny particles of respiratory material become suspended in the air (called aerosols). Such particles may remain suspended and stay infectious for varying periods of time. They are particularly dangerous because their size (1 to 5 microns) allows them to be drawn deep into the lungs and retained. Tuberculosis is spread this way, as is measles in certain settings such as doctors' offices. Air may also spread particles of various sizes from contaminated soil, or from objects such as clothing and floors.

E. Portals of Entry

The portal of entry into the host is usually the same as the portal of exit from the reservoir.

In some diseases, however, the exit and entry portals may differ. Example: staphylococcal bacteria may escape from one person's respiratory tract to infect another person's skin lesion. If that person is a foodhandler, the staphylococcal bacteria may escape from the infected skin lesion, contaminate food where it can incubate, and cause "food poisoning" in people eating the food.

F. Susceptible Host

The last essential component in the chain of infection is the susceptible host. Susceptibility is affected by:

- Genetic factors
- General resistance factors
- Specific acquired immunity

1. **<u>Genetic factors</u>** The role of *genetic factors* in susceptibility to infectious diseases is not yet well understood. Genes do seem to play a role in the progression of HIV disease, and perhaps in individuals' susceptibility to meningococcal meningitis.

2. **<u>General resistance factors</u>** include many body functions that we take for granted. Intact skin and mucous membranes help us resist disease. So do the gastric acid in our stomachs, the cilia in our respiratory tracts, and the cough reflex.

3. **<u>Specific acquired immunity</u>** is the greatest influence on host susceptibility. This immunity is specific to a particular disease agent, and it may be acquired <u>naturally</u> or <u>artificially</u>.

- <u>Natural immunity</u> may be acquired by experiencing an infection, which is called "active natural immunity." Many diseases confer immunity after a single infection, but many others do not. A single bout of measles or chickenpox, for example, confers lifelong immunity to that disease. Influenza and salmonella are examples of infections that do not confer immunity and therefore may recur.

  Another mechanism of natural immunity is the transfer of antibodies from the mother to the newborn child, via the placenta and/or breast milk. This is called "passive natural immunity," and it diminishes after varying lengths of time. It is very important in giving infants a good head start in life.

- <u>Artificial immunity</u> may be acquired through the use of vaccines, toxoids and immune globulins.
  - Active immunity: Receiving a vaccine or toxoid stimulates "active" immunity, since the recipient responds by producing his/her own antibodies.
  - Passive immunity: Receiving an antitoxin or immune globulin confers "passive" immunity, essentially by borrowing the antibodies of other people. Passive immunity lasts for only a short time, while active immunity usually lasts much longer, even for a lifetime.

III. The Infectious Disease Spectrum

By now, you probably appreciate the complexity of the factors that work together to cause the transmission of infectious agents. The *impact* of disease agents on human host populations is also a bit complex.

If a large number of individuals are equally exposed to an infectious agent, they do not all respond in the same manner. In fact, there may be a broad range of responses:

- Some do not become infected at all
- Some become infected but develop no symptoms
- Some become infected and develop mild or moderate symptoms
- Some become infected and develop severe symptoms
- Some die as a result of their infection

Part of this variation is due to the capacity of the agent to produce disease. Infection of a healthy adult population with salmonella is likely to result in mostly inapparent or mild cases, with only a few people with more severe symptoms and very few deaths. On the other end of the spectrum, infections with rabies almost always result in severe illness and death.

Part of the variation is due to differing levels of resistance of the hosts. If measles is introduced into a highly immunized population, then most individuals do not become infected. If measles is introduced into an unimmunized, nutritionally deprived population, the spectrum shifts toward severe symptoms and a high death rate.

The existence of the infectious disease spectrum can make it challenging to find out the extent of transmission in a particular population. Most cases with inapparent or mild symptoms will never be discovered or reported, since these people will not seek health care. So when moderate or severe cases are reported, they may represent the "tip of the iceberg."

Another challenge is posed by the fact that many diseases look alike. A variety of agents may produce essentially similar clinical syndromes. For example, the signs and symptoms of tuberculosis, other mycobacteria, and histoplasmosis may be the same. However, effective treatment and control measures are very different for these three diseases. This is why laboratory identification of the specific disease agent is so important in any epidemiological investigation.

Summary

In order for infection and disease to occur in an individual, a process involving six related components must occur. This process has been referred to as the "Chain of Infection."

To stop the spread of disease, one or more of these links must be broken.

The impact of disease agents on human host populations is complex. If a large number of individuals are equally exposed to an infectious agent, there may be a broad range of responses, from no infection at all to death.

Because of the infectious disease spectrum, it can be challenging to identify the extent of transmission in a particular population.

Many diseases share the same signs and symptoms, so laboratory studies are important to identify the specific disease agent.